

In the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Upon entry of the present amendment, the claims will stand as follows:

Please cancel claims 3, 10-12, 28, and 44 without prejudice.

Please amend claims 1, 2, 6, 7, 13, 14, 16-19, 21, 23, 24, 29, 34, 39, and 43 as follows:

1. (Currently Amended) A method for enhancing capacity of ~~impaired~~ bone marrow [[cells]] to promote development of collateral blood vessels in a patient ~~in need~~ having a condition that impairs naturally occurring angiogenic processes as compared with that found in young healthy individuals, said method comprising:

growing ~~the impaired~~ bone marrow cells under suitable culture conditions in a suitable growth medi[[a]]um for a period of time sufficient to promote production by the bone marrow cells of early attaching cells;

transfecting at least a portion of the early attaching cells with an adenovirus vector comprising a polynucleotide that encodes one or more agents selected from angiogenic cytokines, growth factors and mammalian angiogenesis promoting factors hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS), and

culturing the transfected early attaching cells ~~so as to allow production of~~ in a culture medium to produce the one or more agents and conditioned medium,

thereby enhancing capacity of the ~~impaired~~ bone marrow cells and/or the conditioned medi[[a]]um ~~derived from these cells while being grown in culture~~ to promote development of collateral blood vessels in the patient into which the cells and/or the conditioned medi[[a]]um are delivered as compared with that of either non-transfected cells or conditioned medi[[a]]um similarly obtained using non-transfected early attaching cells ~~grown in culture~~.

2. (Currently Amended) The method of claim 1, wherein the ~~bone marrow cells are~~ impaired by disorder is donor aging.
3. (Cancelled)
4. (Original) The method of claim 1, wherein the disorder is hypercholesterolemia.
5. (Original) The method of claim 1, wherein the donor is the patient.
6. (Currently Amended) The method of claim 1, wherein the cells are grown ~~in culture~~ for about 12 hours to about 12 days.
7. (Currently Amended) The method of claim 1, wherein the cells are cultured for period of ~~time is from~~ about 12 hours to about 3 days.
8. (Original) The method of claim 1, further comprising obtaining bone marrow from a donor and filtering the bone marrow to obtain the bone marrow cells.
9. (Original) The method of claim 8, wherein the filtering removes particles larger than from about 300 μ to about 200 μ .
10. (Cancelled)
11. (Cancelled)
12. (Cancelled)

13. (Currently Amended) The method of claim 1[[2]], wherein the agent is selected from PR39, a FGF and a NOS.
14. (Currently Amended) The method of claim 1, further comprising stimulating the transfected early attaching cells by contact with HIF-1 or EPAS1-1 or by exposure to hypoxia.
15. (Original) The method of claim 1, wherein the cells are marrow-derived stromal cells.
16. (Currently Amended) The method of claim 15, wherein the conditioned medi[[a]]um is ~~derived~~ produced by culturing the marrow-derived stromal cells.
17. (Currently Amended) A method for enhancing collateral blood vessel formation in heart or limb tissue of a patient in need thereof, said method comprising:
- obtaining autologous bone marrow from the patient;
 - growing the autologous bone marrow in a suitable medium under suitable culture conditions ~~in a container~~ for a period of time sufficient to promote production by the bone marrow of early attaching cells;
 - transfecting at least a portion of the early attaching cells with an adenovirus vector comprising a polynucleotide that encodes one or more agents selected from ~~factors~~ hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), a fibroblast growth factor (FGF), a NOS, and PR39 so as to cause expression of the one or more agents to produce conditioned medium; and
 - directly administering to a ~~desired~~ site of impaired blood flow in heart or limb tissue of the patient an effective amount of the transfected early attaching cells and/or the conditioned medi[[a]]um ~~derived from the transfected cells while being grown in culture,~~
thereby enhancing to enhance collateral blood vessel formation at the site in the patient.

18. (Currently Amended) A method for enhancing collateral blood vessel formation in heart or limb tissue of a patient in need thereof, said method comprising:

growing bone marrow under suitable culture conditions for a period of time sufficient to promote production by the bone marrow of early attaching cells;

transfecting at least a portion of the early attaching cells with an adenovirus vector comprising a polynucleotide that encodes one or more agents selected from angiogenic cytokines, growth factors and mammalian angiogenesis-promoting factors for expression by the early attaching cells; and

culturing the transfected early attaching cells in a culture medium and for a time suitable to allow expression by the cells of the one or more agents, ~~thereby producing~~ to produce conditioned medium; and

directly administering to a desired site of impaired blood flow in heart or limb tissue of the patient an effective amount of the transfected early attaching cells and/or the conditioned medium;

~~thereby enhancing~~ to enhance collateral blood vessel formation at the site in the patient.

19. (Currently Amended) The method of claim 18, wherein the early attaching cells are marrow-derived stromal cells and the cells are directly administered to a site of ischemia in the patient or adjacent thereto.

20. (Original) The method of claim 18, wherein the early attaching cells are marrow-derived stromal cells and the conditioned medium is directly administered to a site of ischemia in the patient.

21. (Currently Amended) The method of claim 18, wherein the cells and/or the conditioned medium are injected into the blood stream for ~~administration~~ delivery to the site.

22. (Original) The method of claim 20, wherein the cells and/or the conditioned medium are injected into an artery supplying the site.

23. (Currently Amended) The method of claim 18, wherein the period of [[time]] growing is from about 3 [[hours]] days to about 12 days.

24. (Currently Amended) The method of claim 23, wherein the period of [[time]] culturing is from about 3 hours to about 3 days.

25. (Original) The method of claim 18, further comprising filtering the bone marrow prior to culturing of the bone marrow to obtain the early attaching cells.

26. (Original) The method of claim 25, wherein the bone marrow is autologous bone marrow.

27. (Original) The method of claim 18, wherein the agent is a transcription factor that promotes mammalian angiogenesis.

28. (Cancelled)

29. (Currently Amended) The method of claim [[2]]18, wherein the agent is selected from a fibroblast growth factor (FGF), a NOS, and PR39 .

30. (Original) The method of claim 29, wherein the agent is selected from FGF-1, FGF-2, FGF-4, and FGF-5.

31. (Original) The method of claim 29, wherein the agent is selected from inducible NOS and endothelial NOS.

32. (Original) The method of claim 29, wherein the agent is PR39.
33. (Original) The method of claim 18, wherein the transfected cells are injected directly into heart or leg muscle to promote angiogenesis therein.
34. (Currently Amended) The method of claim 18, wherein the method enhances collateral blood vessel formation in the heart or leg muscle.
35. (Original) The method of claim 18, wherein the method promotes development of newly implanted myocardial cells.
36. (Original) The method of claim 18, wherein the method promotes electrical conductivity of the heart of a patient with cardiac electrical pathway impairment.
37. (Original) The method of claim 18, wherein the method enhances myocardial function in a patient with impaired myocardial function.
38. (Original) The method of claim 18, wherein the method treats a left or right ventricular condition causing impaired heart function in the heart of the patient.
39. (Currently Amended) A therapeutic composition comprising early attaching cells derived from bone marrow, which cells have been transfected with an adenoviral vector comprising a polynucleotide that encodes one or more agents selected from ~~angiogenic cytokines, growth factors and mammalian angiogenesis promoting factors~~ hypoxia inducing factor-1 (HIF-1), endothelial PAS domain protein 1 (EPAS1), Monocyte Chemoattractant Protein 1 (MCP-1), granulocyte-monocyte colony stimulatory factor (GM-CSF), PR39, a fibroblast growth factor (FGF), and a nitric oxide synthase (NOS).

40. (Original) The therapeutic composition of claim 39, further comprising conditioned medium in which the cells have been grown in culture for a time sufficient to allow expression of one or more of the agents.

41. (Original) The composition of claim 39, wherein the polynucleotide further comprises a transcription regulatory region operatively associated with the polynucleotide.

42. (Original) The composition of claim 39, wherein the transfected cells have been stimulated by exposure to hypoxia.

43. (Currently Amended) The composition of claim 39, further comprising heparin or another anticoagulant.

44. (Cancelled)

45. (Original) The composition of claim 39, wherein the early attaching cells are marrow-derived stromal cells.

46. (Original) The composition of claim 39, wherein the composition is intended to be injected into a patient having ischemic tissue and the early attaching cells are derived from bone marrow obtained from the patient.